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Acute stress impairs self-control in goal-directed choice by altering multiple functional connections within the brain's decision circuits

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**Acute stress impairs self-control in goal-directed choice by altering
multiple functional connections within the brain's decision circuits**

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Summary

Important decisions are often made under stressful circumstances that might compromise self-regulatory behavior. Yet the neural mechanisms by which stress influences self-control choices are unclear. We investigated these mechanisms in human participants who faced self-control dilemmas over food rewards while undergoing fMRI following stress. We found that stress increased the influence of immediately rewarding taste attributes on choice and reduced self-control. This choice pattern was accompanied by increased functional connectivity between ventromedial prefrontal cortex (vmPFC) and amygdala and striatal regions encoding tastiness. Furthermore, stress was associated with reduced connectivity between the vmPFC and dorsolateral prefrontal cortex regions linked to self-control success. Notably, alterations in connectivity pathways could be dissociated by their differential relationships with cortisol and perceived stress. Our results indicate that stress may compromise self-control decisions by both enhancing the impact of immediately rewarding attributes and reducing the efficacy of regions promoting behaviors that are consistent with long-term goals.

Introduction

Choices between the temptation of immediate gratification and better long-term outcomes are a frequent occurrence in daily life. The ability to forgo an immediate or salient reward in order to achieve another goal (i.e. self-control) has been linked to a person's physical, social, and economic well being (Duckworth, 2011; Moffitt et al., 2011). Given the importance of self-control abilities in many facets of life, recent studies have begun to examine the neurobiology of self-control (Crockett et al., 2013; Hare et al., 2009; Hare et al., 2014; Kable and Glimcher, 2007; Luo et al., 2012; McClure et al., 2004; van den Bos et al., 2014), but thus far, these investigations have generally examined self-control choices in carefully controlled settings designed to minimize participant discomfort or stress. In reality, however, many important decisions are made during or immediately following stressful events that occur regularly in daily life (Smyth et al., 1998). Experimental data demonstrate that stress can have both immediate and long-lasting effects on brain and behavior (Duckworth et al., 2012; Kandasamy et al., 2014; Lewis et al., 2014; McEwen and Morrison, 2013; Schwabe and Wolf, 2010). Even relatively moderate and acute stressors have been shown to affect decision-making (Gathmann et al., 2014; Lempert et al., 2012; Porcelli and Delgado, 2009; Porcelli et al., 2012; Schwabe et al., 2012; Schwabe and Wolf, 2009; Starcke et al., 2008). However, the neurobiological effects of stress on the important class of choices involving temptation and self-control remain unknown. Here, we examined the impact of acute stress on brain activity during self-control choices over primary food rewards and show that it caused multiple changes in the brain's decision circuitry that can be linked to either cortisol levels or the perception of being stressed.

Previous studies on the neuroendocrine and behavioral consequences of stress suggest that acute stress could affect choices requiring self-control in at least two ways. Stress has been claimed to impair prefrontal functions such as directing attention and inhibiting inappropriate actions, which would be fundamental for goal-based control of actions and self-control (Arnsten, 2009; Starcke and Brand, 2012). At the same time, stress has been reported to amplify “craving” or “wanting” signals that might bias an individual towards choosing immediately rewarding options (Adam and Epel, 2007; Pruessner et al., 2004; Sinha et al., 1999). Therefore, we hypothesized that acute stress would impair self-controlled decisions in favor of actions leading to salient and proximal rewards through one or a combination of these two mechanisms.

To test this hypothesis, we combined an acute stress manipulation with a self-control decision paradigm and investigated the neural mechanisms underlying the predicted stress-induced focus on immediately rewarding options. Specifically, we used a previously established self-control task involving binary choices between primary food rewards that varied on the attributes of healthiness and taste (Hare et al., 2009) in combination with the Socially Evaluated Cold Pressor Test (Schwabe et al., 2008) as a means of stress induction (Figure 1 and Experimental Procedures). Using multi-attribute food stimuli allowed us to disentangle the brain’s reaction to long-term benefits, such as pursuing a goal of eating healthy, and short-term rewards, for example the pleasurable taste experienced immediately upon eating the food. In addition to the stimuli themselves, we added a choice recommendation on a subset of trials

to test how such external information might interact with acute stress to affect self-control. We told participants that the recommended items would be the healthier option in most trials, but that sometimes the recommendation would mislead them towards the less healthy food and, in such cases, they should override the recommendation to maintain their health goal. Consistent with our hypothesis, we found that stressed participants' choices were more affected by short-term taste rewards, and that they encoded taste more strongly in portions of the amygdalae (Amyg) and ventral striatum (vStr). Furthermore, the stress manipulation increased task-dependent connectivity between these limbic regions and a portion of the ventromedial prefrontal cortex (vmPFC) that represented integrated stimulus value. This increased connectivity between vmPFC and Amyg and Str was more strongly correlated with salivary cortisol levels, an indicator of the hypothalamic-pituitary-adrenal (HPA) axis stress response, than with self-reported ratings of stress. In addition, increased stress levels were also associated with decreased connectivity between vmPFC and dorsolateral prefrontal cortex (dlPFC) regions that were activated when engaging self-control. However, in this case the changes in vmPFC-dlPFC connectivity were more strongly associated with self-reports of perceived stress level than salivary cortisol. Thus, these two alterations in task-dependent functional connectivity within the decision network are differentially related to the HPA axis responses and psychological perceptions following acute stress. Together these findings demonstrate that acute stress induction results in parallel, and at least partially dissociable, alterations to neural decision circuits incorporating both appetitive motivation and behavioral regulation that may

combine to impair the brain's ability to exercise self-control in the face of temptations.

Results

Stress manipulation

We recruited individuals who reported making an effort to maintain a healthy lifestyle in terms of diet and exercise, but who still enjoyed and often consumed junk food and thus often faced a self-control challenge in our choice task (see Supplemental Experimental Procedures). These participants were randomly assigned to undergo the stress induction or control procedure before the decision task. Participants in the Stress group reported higher perceived stress levels (PSL) on a visual analog scale (anchors: 0, “not at all” and 100, “extremely”) immediately after the SECPT stress induction procedure than those reported in the Control group following the control procedure ($Z = 2.03$, one tailed $p = .02$; see Figure 2A). The Stress and Control groups did not differ significantly on any other mood ratings, but the Stress group reported lower hunger levels (see Table 1 and Supplemental Experimental Procedures). Including hunger level as a control did not change any of the differences in choice behavior described below. In addition to self-report measures of experienced stress, we analyzed salivary cortisol concentrations as an indicator of the activity in the HPA axis following our acute stress manipulation. Figure 2B shows that the stress induction procedure resulted in higher maximum cortisol levels ($Z = 2.19$, one tailed $p = 0.01$) and total cortisol responses (area under the curve (AUC): $Z = 1.87$, one tailed $p = 0.03$) than our control procedure. Furthermore, participants in the Stress group maintained an elevated cortisol level compared

to baseline ($Z = 2.18$, one tailed $p = .02$) until the end of the behavioral task (+45 minutes). Lastly, the correlation between individual participant's PSL and AUC cortisol levels was positive, but not significant ($r = 0.17$, $p = 0.26$).

Behavior

Food consumption decisions were based more strongly on the tastiness of each option for participants in the Stressed compared to Control groups. On every trial, participants selected one of two food items (i.e. left or right) to potentially eat following the fMRI scan (see Fig. 1 and Experimental Procedures). A logistic regression analysis testing the influence of health, taste, and recommendations on the probability of choosing the item on the left side of the screen demonstrated that, although healthiness had the strongest overall influence on choice in both groups, (Figure 2C), Stressed participants put a higher weight on the taste of the food items (taste left (i.e. chosen) $t_{49} = 2.13$, $p = 0.04$; taste right (i.e. non-chosen) $t_{49} = -2.30$, $p = 0.03$) than Controls. However, this analysis of choices across all trials does not distinguish between decisions in which health and taste attributes are aligned and trials in which the tastier item is less healthy.

To examine the effects of acute stress on self-control behavior more directly, we tested the probability of self-control failure (choosing a more tasty, less healthy item) in the subset of trials where health and taste attributes were in conflict because the healthier item was less tasty. The participants' decisions on this subset of self-control challenge trials were correlated with their reports of restricted eating behavior in every-day life, such that those with more restricted eating habits made more frequent self-control choices during the task ($r = 0.30$,

$p = 0.03$). To compare choice behavior on these trials between the Stress and Control groups, we computed a generalized linear mixed-effects model including regressors for the absolute differences between the chosen and non-chosen food items in health (H_{diff}) and taste (T_{diff}), the recommendations on each trial and the interactions of H_{diff} , T_{diff} , and recommendation with group. Consistent with the analysis over all trials, this regression demonstrated that greater differences in taste between the two options resulted in more self-control failures for stressed participants compared to controls (Fig. 3A; $Z = 4.53$, $p = 6.05\text{e-}06$), with the Stress group failing 24% more often than controls on trials with the most extreme differences in taste. In addition, there were main effects of H_{diff} ($Z = -13.87$, $p < 2\text{e-}16$), T_{diff} ($Z = 6.96$, $p = 3.5\text{e-}12$), and recommendation ($Z = -10.12$, $p < 2\text{e-}16$) across both groups.

Next, we examined how individual differences in cortisol and perceived stress levels related to choice by extending the regression model above to include cortisol (measured as total AUC) and PSL as well as their interactions with all other factors (see Experimental Procedures and Table S1A). This extended analysis again revealed main effects of H_{diff} ($Z = -11.09$, $p < 2\text{e-}16$), T_{diff} ($Z = 5.74$, $p = 9.34\text{e-}9$), and healthy recommendations ($Z = -7.39$, $p = 1.49\text{e-}13$) across all participants, as well as an interaction between Stress group and T_{diff} ($Z = 4.23$, $p = 2.38\text{e-}05$). In addition, there were significant interactions for PSL X H_{diff} ($Z = 2.84$, $p = 0.01$), and PSL X healthy recommendations ($Z = 2.47$, $p = 0.01$) such that both were less effective in promoting self-control. Moreover, there was a three way interaction between PSL, Stress group, and T_{diff} ($Z = 2.40$, $p = 0.02$), such that stressed participants reporting the strongest feelings of stress were

most sensitive to taste attributes. Higher levels of cortisol also reduced the degree to which healthy recommendations facilitated self-control ($Z = 2.31$, $p = 0.02$) and there was another three way interaction between cortisol, PSL, and T_{diff} ($Z = 2.19$, $p = 0.03$), indicating that higher levels of both cortisol and PSL increased the degree to which taste attributes were associated with self-control failures. Thus both individual PSL and cortisol levels explained additional variance in participants' choice behavior beyond the differences linked to the stress induction procedure overall.

We also investigated the effects of stress on choice reaction times (RTs; Table S2, See Supplemental Information for full details). These RT effects were consistent with the choice data in showing a greater impact of taste on behavior (i.e. faster reaction times) in participants with higher PSL and cortisol levels ($t = -3.51$, $p < 0.0004$). However, there was also a main effect of self-control failure such that all participants were slower when choosing a tastier, but less healthy option ($t = 4.20$, $p < 0.00003$) indicating that these choices were not simply the result of response inhibition failures, which should result in faster reaction times (see also Table S3 for further analyses related to response inhibition).

fMRI

In order to examine how acute stress influenced the brain's decision circuitry, we analyzed BOLD activity measured during the choice task using a series of general linear models.

First, we tested for regions that reflected the value of food items at the time of choice by computing a model (GLM-FV) that included parametric regressors

representing the subjective value of the chosen and non-chosen food item on each trial. The subjective value of food items was computed by combining the weighted values for the taste and health of each food. These weights were derived from the logistic regression summarized in Fig. 2C and were determined individually for each participant (see Experimental Procedures for details). We found that vmPFC and several other regions represented the integrated subjective value of the chosen food for both Stressed and Control groups as well as the relative value difference between the chosen and non-chosen options (Table S4; $p < .05$, whole brain FWE corrected). There were no brain regions that significantly differed in their representations of subjective food value between the Stressed and Control participants after correcting for multiple comparisons. Moreover, a post-hoc two-sample t-test revealed no significant difference between groups in the vmPFC ROI used as a seed in subsequent analyses presented below ($t_{49} = -0.80$, $p = 0.42$). These results suggest that acute stress did not fundamentally change the circuits involved in overall subjective value computation that have been reported by numerous studies across a wide range of decision contexts (Bartra et al., 2013; Clithero and Rangel, 2013).

Next, motivated by the behavioral finding that stressed participants' decisions were biased towards the taste of food items, we investigated the representation of relative taste value (taste of chosen item – taste of non-chosen item) in Stressed versus Control participants (see GLM-HT in the Experimental Procedures). We were particularly interested in the vStr and Amyg given that these limbic structures contain high densities of glucocorticoid receptors (GR) (Ahima et al., 1991; Zoli et al., 1990), and play important roles in signaling the

salience and motivational value of stimuli (Bartra et al., 2013; Cooper and Knutson, 2008; Everitt et al., 1989; Jenison, 2014; Litt et al., 2011). Consistent with a role in signaling motivational value, the bilateral Amyg and right nucleus accumbens, a substructure of the vStr, reflected the relative taste value of chosen options more strongly in Stressed compared to Control participants (Fig. 3B; $p < 0.05$, small volume corrected (SVC); Table S5). An exploratory whole brain analysis revealed no further differences in relative taste encoding between Stressed and Control participants in other areas of the brain. Individual PSL and cortisol levels did not explain additional variance in taste related activity within Amyg and vStr beyond the stress induction procedure, however separating participants along a median split for cortisol level yields results that are qualitatively similar to the Stress versus Control group comparison (Fig. S1A).

In addition to testing for local representations of taste value, we examined changes in functional connectivity (psychophysiological interactions (PPI)) when participants chose tastier items. Specifically, we tested whether connectivity with the vmPFC node of the valuation system identified in GLM-FV differed between Stressed and Control participants during choices in which they selected the tastier item, controlling for connectivity during choices for healthier items. We focused on the vmPFC as a seed because of previous work highlighting the central role of this region in goal-directed choice in general (Bartra et al., 2013; Clithero and Rangel, 2013) and specifically during self-regulated choice (Hare et al., 2009; Hare et al., 2014). We found that positive connectivity between vmPFC and portions of our Amyg/vStr region of interest was greater in Stressed versus Control participants when choosing the tastier item (Fig. 4; $p < .05$ SVC). A whole

brain analysis revealed that the Stress group showed greater vmPFC connectivity with several brain regions including the Amyg, vStr, and bilateral insula during tastier choices (Table S6; $p < .05$, whole brain FWE corrected). Furthermore, using a multiple regression analysis, we found that the increase in vmPFC connectivity during tastier choices was more strongly correlated with individual cortisol levels compared to self-reported PSL in the striatum and extended amygdala (Fig. 5C-D; Table S7; $p < .05$, whole brain FWE corrected).

The stronger encoding of relative taste value in areas such as Amyg and vStr that signal the motivational value of objects (Miller et al., 2013), together with their greater functional connectivity to vmPFC at the time of a tastier choice, suggests a potential mechanism for increasing the importance of taste in the value computation processes (Hampton et al., 2007; Jenison, 2014; Rudebeck et al., 2013), and subsequently in the observed choices of the stressed participants, especially those with a stronger HPA axis response to the stressor. It may be that acute stress results in enhanced reward salience or stronger “wanting” (Berridge, 1996; Mahler and Berridge, 2011) for more tasty items and that these motivational signals influence decision processes.

Beyond the intrinsic taste and health attributes of each food, choices and RTs in both groups were influenced by the healthy and unhealthy recommendations. In order to further investigate choices representing the strongest self-control challenges, i.e. refusing a recommended tastier and less healthy food, we ran an additional model (GLM-OR) to test for brain areas that were associated with overcoming both misleading recommendations (i.e. inconsistent with the goal of

eating healthy) and conflicting taste preferences in order to choose the healthier option. These trials represent the strongest self-control challenges because both taste preferences and recommendations promote the goal-inconsistent option. Recall that despite the enhanced signaling of relative taste value in motivation and reward circuits, participants in the Stress group often still chose the healthier item. Across both Stressed and Control groups, activity in left dorsolateral prefrontal cortex (dlPFC), dorsal anterior cingulate cortex (dACC), and the left superior parietal lobule (SPL) was greater when participants successfully overrode a misleading recommendation and chose the healthier, but less tasty option ($p < .05$, whole brain FWE corrected; Table S8). There were no regions whose activity significantly differed between the Stress and Control groups when participants successfully overrode misleading recommendations (but see Table S9).

Next, we repeated our comparison of the relationship between individual differences in PSL and cortisol levels and vmPFC connectivity, but this time when choosing the healthier over the tastier option. To that end, we calculated the difference in connectivity during healthier versus tastier choices over all participants. This subtraction contrast measures increases in connectivity during choices for food items that are healthier, but less tasty than the alternative (i.e. choices that required self-control). Applying the same multiple regression analysis we used for connectivity during tastier choices revealed that the degree of negative connectivity between vmPFC and dlPFC decreased as a function of participants' PSL ratings and was more closely associated with PSL than cortisol levels (Fig. 5A-B; $p < .05$, whole brain FWE corrected; Table S10). Note that this

negative connectivity between left dlPFC and vmPFC is consistent with previous reports on the neural mechanisms of self-control when overcoming taste temptations (Hare et al., 2009). Thus, while vmPFC connectivity with Amyg and vStr during tastier choices was associated with cortisol levels and not PSL, the opposite relationship holds for vmPFC-dlPFC connectivity during healthier choices. This connectivity is correlated with PSL, but not cortisol. The dissociable links to PSL and cortisol suggest that distinct aspects of the acute stress response alter these two pathways in the decision network during self-control choices.

Discussion

Our findings indicate that stress biases the decision process in the brain by altering two pathways: one that might signal information about the stimulus (e.g. taste), and another that has been linked to context and goal maintenance (e.g. choosing healthy food). At the level of observed choices, we found that stressed participants had an increased preference for immediately rewarding stimulus attributes and that this preference increased as a function of individual perceived stress and cortisol levels. The neuroimaging data complement this behavioral finding and show that acute stress induction results in alterations to multiple nodes of a decision-making network that converges to represent the overall value of stimuli in the vmPFC. However, the similar effects of increased PSL and cortisol on decisions can be dissociated at the neural level by their effects on vmPFC-dlPFC and vmPFC-Amyg/vStr functional connectivity, respectively.

Acute stress induction led to a stronger influence of taste attributes on choice that was paralleled by changes in activity and connectivity patterns in Amyg and vStr. Participants in the Stress group showed stronger correlations between the relative tastiness of the chosen option and BOLD activity in the Amyg and vStr compared to Controls. In addition, we observed that the positive coupling of Amyg and vStr with vmPFC was associated with more immediately rewarding, taste-oriented choices, consistent with previous findings showing that activity in vStr is associated with immediate reward selection (Hariri et al., 2006). Moreover, there was a significant positive correlation between higher cortisol levels and increased connectivity between vmPFC and Amyg/vStr when choosing a tastier food, but no relationship between this increased connectivity and PSL. This dissociation suggests that the HPA axis response to stress can have effects on neural decision circuits that are distinct from those associated with the subjective perception of being stressed. Enhanced positive coupling between vmPFC and Amyg and vStr regions may indicate the propagation of a stronger motivational signal for the tastier item into value computations. However, although previous studies have shown that activity in these areas can influence reward value coding in vmPFC regions (Hampton et al., 2007; Jenison, 2014; Rudebeck et al., 2013) we note that the PPI analyses we conducted do not indicate the direction of signaling between regions or the presence of monosynaptic connections. Overall, these results are consistent with the idea that these Amyg and vStr signals may be linked to the influence of taste on valuation and choice.

In addition to the effects of our acute stress induction on the HPA axis and Amyg and vStr activity, we observed individual differences in the subjective perception of being stressed that correlated with self-control at the behavioral and neural levels. Specifically, we observed that as PSL increased, larger taste differences between options resulted in more self-control failures. Furthermore, participants with higher PSL were less likely to follow the health goal when it mattered most (i.e. when there was a large difference in healthiness) than lower PSL participants. These affects of PSL on behavior were paralleled by differences in connectivity between dlPFC and vmPFC when participants chose healthier over tastier options. In addition to the altered coupling between vmPFC and Amyg/vStr, we identified a second signaling pathway between vmPFC and dlPFC that showed a reduction in negative connectivity for participants with high PSL. Prior work (Hare et al., 2009; Harris et al., 2013) suggests that this dlPFC-vmPFC connection may help to modulate value comparisons and to integrate taste and health attributes in the vmPFC. A weaker modulatory connection with dlPFC might result in less effective down-regulation of the impact of the taste signaling, resulting in a relative weighting for taste attributes in vmPFC that is too high given the health goal. We speculate that decreased modulation from dlPFC in combination with stronger limbic inputs may combine to create the taste influence that we observed to be more pronounced in stressed participants than in controls. This is consistent with our behavioral finding that individuals with higher levels of both perceived stress and cortisol are most likely to fail on difficult (i.e. high taste difference) self-control trials (PSL X cortisol X T_{diff} interaction) and that PSL and cortisol levels are linked to dlPFC and Amyg/vStr connectivity with vmPFC, respectively. Thus, stressed participants might be less

willing to forego a bit of pleasure (taste) in favor of advancing their health goal because they have both a stronger taste signal entering the valuation process in vmPFC, and less effective levels of connectivity between dlPFC and vmPFC compared to control participants.

Although the neurobiological effects of stress on self-control choices over secondary rewards remain unknown, it has been shown that stress affects goal-directed choices over both primary and secondary rewards. The biasing of the valuation system towards immediate rewards we observed following stress may be a means of trying to maintain allostatic balance. It is interesting to consider our results in light of previous findings showing that the consumption of rewarding stimuli (e.g., palatable food) may help down-regulate physiological stress reactions, in both rodents and humans (Adam and Epel, 2007). Such drives may be particularly strong in the context of self-control choices over primary food rewards. However, stress has also been reported to compromise goal-directed contributions to choices over monetary rewards, biasing humans towards habitual actions (Otto et al., 2013; Schwabe and Wolf, 2009; Schwabe and Wolf, 2010; Soares et al., 2012). When viewing cues or anticipating monetary outcomes, stressed individuals show greater activity in reward regions including the amygdala, striatum, and medial prefrontal cortex (Dagher et al., 2009; Kumar et al., 2014), and acute psychosocial stress may increase dopamine levels in the vStr (Pruessner et al., 2004). Stress also alters risk preferences during monetary gambles in humans (Putman et al., 2010; Starcke et al., 2008; van den Bos et al., 2009), and can change the perception and influence of reward at the time of consumption (Lewis et al., 2014; Porcelli et al., 2012; Preston et al., 2007;

Putman et al., 2010; Schwabe et al., 2012; Schwabe and Wolf, 2010; Starcke and Brand, 2012). Moreover, stress has been associated with aggravating addiction processes (Ansell et al., 2012; Koob and Le Moal, 2008). A common theme across many studies of acute stress is that it makes the individual more focused on the present situation. A present bias would be sensible given that throughout evolutionary history, stress has generally occurred in situations in which an acute physical or social threat must be managed in order to ensure survival or status in a group. In such a situation, coping with the stressor and stress reaction should be prioritized. Given a constraint of limited resources, this means that achieving less pressing long-term goals would need to wait until the stressful situation has been resolved.

Stressful events that may alter behavior remain a common occurrence in modern life. Experience sampling studies have shown that stressful events occur frequently in daily-life and even modestly taxing events have a significant impact on HPA activity and self-reported measures of stress (Jacobs et al., 2007; Smyth et al., 1998; Van Eck et al., 1996). The HPA and psychological indicators of stress found in our participants following the SECPT are in line with the levels reported in previous studies of daily-life stress responses. Following the SECPT stress induction, participants reported a mean perceived stress level of 33%, and had a mean salivary cortisol level of approximately 9 nmol/liter 25 minutes after the stressor. These values are in line with ratings and cortisol levels reported by Smyth et al., (1998) who collected reports of recent and anticipated stressors during the standard daily activities of 120 participants over the course of two consecutive days (24 samples per participant in total). These participants

reported recent and anticipated stressors (e.g. family issues, personal relationships, financial and work-related problems) on more than 20% of sampled time points. These experiences were rated as 47% of maximum stress and produced cortisol responses of between 8-9 nmol/liter after 25 minutes depending on the number of concurrent stressors reported. These findings show that stressors unrelated to a specific decision occur with ample frequency in daily life, and as we demonstrate, may influence the response to self-control challenges that arise in close proximity to these stressful events.

The individual reaction to stress depends largely on a person's appraisal of the situation as well as their state of physical health (McEwen, 1998). Our results demonstrate that the effects of stress on self-regulatory behavior are driven at least in part by psychological perceptions of stress that can be dissociated from cortisol responses at the neural level, and have potential implications for diseases such as obesity, addiction, and other pathological behaviors exacerbated by stress. The effects of stress can be increased by overconsumption of tobacco, alcohol, and a rich diet, but can be reduced by healthy activities such as exercise (McEwen, 1998). Therefore, stress response and self-control abilities may be coupled in a feedback loop: healthy dietary choices and exercise may help to regulate the stress response, while past self-control failures (e.g. overeating) may result in stronger present stress responses that again spur the drive to choose less healthy activities. Thus, treatments that promote effective coping strategies may help to prevent the detrimental effects of stress on self-control decisions by reducing perceived stress and its influence on choice behavior. Testing the degree to which the neural mechanisms underlying the

impact of stress on self-regulation that we have identified here generalize to specific clinical populations and other healthy cohorts differing in age, sex, education, or other variables associated with stress sensitivity and self-control will be an important avenue for future studies designed to systematically address these factors.

Beyond determining the effects of acute stress on self-control behavior, our data highlight the importance of multiregional interactions in effectively executing self-control. Previous work has shown that activity patterns within and interactions between valuation and control regions are correlated with individual differences in self-control (Boettiger et al., 2007; Hare et al., 2009; Hare et al., 2014). Others have reported that inhibition of putative control regions via transcranial magnetic stimulation leads to behavioral changes in choices that may require self-control (Figner et al., 2010), but have not shown how this affects the network beyond the area of stimulation. Our acute stress manipulation resulted in altered activity patterns in a number of brain regions and demonstrates that self-control in the context of value-based choice is maintained through a careful balance of connectivity within value computation systems and that the disruption of this balance leads to impairments in self-control decisions.

Experimental Procedures

Participants

Fifty-one male individuals participated in the study (21 ± 2 years SD), and all participants provided informed consent as approved by the Research Ethics Committee of the Canton of Zurich. Participation eligibility was assessed in brief telephone interviews by the recruitment team of the UZH Economics Department, and eligibility for the study was checked again at the day of testing with a brief questionnaire on exclusion criteria (see Supplemental Experimental Procedures). Participants for this study were selectively recruited to ensure the food choices in our task would represent self-control challenges for them and they would respond similarly to the stress induction (see Supplemental Experimental Procedures). Specifically, we recruited individuals who reported making an effort to eat a healthy diet and exercise regularly, but also still enjoyed and frequently consumed relatively unhealthy junk food items. Participants randomly assigned to the Stress and Control groups did not differ in the self-reported typical weekly mean number of times they consumed fruit and vegetables (Stress = $10.3 \pm$ SD of 3.3, Controls = 10.3 ± 3.0), undertook strength or cardiovascular training (Stress = 3.4 ± 2.2 , Controls = 3.7 ± 1.9), or ate junk food items (Stress = 7.7 ± 3.6 , Controls = 7.6 ± 4.2).

Experiment timeline

Participants spent a total of 3 hours in the lab. They first rated 180 food items for healthiness, tastiness, and their overall appetitive value. Food items were shown as color images on a computer monitor. Participants then completed the SECPT or the control procedure. They were positioned in the scanner directly

afterwards and started working on the food choice paradigm at minute 12-17 after stressor onset, allowing for a cortisol peak measurement right after the first fMRI run, and another measurement after the third run, 40-45 minutes after stressor onset. Each run took 7 minutes, thus the peak of the cortisol measurement was reached during the behavioral task, and cortisol values in the Stress group stayed elevated during the whole scan time compared to the Control group. After the scanning session, participants completed a battery of psychometric questionnaires (see Supplemental Experimental Procedures) and the last saliva measurement, after which they received their chosen food, were debriefed, and paid for their participation.

Stress induction

Stress induction and scanning always took place between 14.00 and 17.00 in the afternoon to account for the diurnal rhythm of cortisol. Twenty-nine participants were randomly allocated to the Socially Evaluated Cold Pressor Test (SECPT, (Schwabe et al., 2008)). Participants had to immerse their hand in an ice water bath (0-4° C) for 3 minutes while being videotaped and monitored by the experimenter. They were instructed not to communicate and were informed the experimenter would indicate when the test was over. Participants were allowed to remove their hand from the water bath any time, but if they did (N=5, see Supplemental Experimental Procedures), they were asked to keep looking into the camera until the 3-minute test time was over and were instructed that they could try re-inserting their hand in the water. In the control condition, 22 participants had to keep their hand in a warm water bath (35-35° C) for 3 minutes while the experimenter was in the room, but did not videotape them.

Choice task

Overall, participants made 210 choices (70 in each run) between two food items that were presented on a screen. Choice screens (3 seconds) were presented with a jittered inter-trial interval of 2-6 seconds. One choice was randomly drawn at the end, and participants had to eat the item they chose in this trial during the 30-minute waiting period. The participants' goal was to choose the healthier of the two items whenever possible, and we reminded them of this goal in between trials with a health symbol in place of the standard fixation cross. In order to test whether an explicitly wrong recommendation (to eat the less healthy item) would affect the behavior of stressed participants, we recommended in 60 trials to choose the less healthy food. In 120 trials, we recommended – in line with the participants' ratings – choosing the healthier item. The remaining 30 trials had no recommendation and served as a baseline. A white frame around the food item indicated our recommendation; when we gave no recommendation, the white frame appeared around the fixation cross (see Fig. 1 and Supplemental Experimental Procedures).

Cortisol, heart rate, and blood pressure measurements

Behavioral pilots with the SECPT indicated that salivary cortisol would peak 20-25 minutes after stressor onset. Therefore, salivary cortisol was collected at minutes +1 after stressor/control offset, and at minutes +25, +45 and +70 after stressor/control onset with a Salivette® swab (Sarstedt, Nümbrecht, Germany), and stored at -20° C until analysis (see Supplemental Experimental Procedures).

Heart rate was measured throughout the stress/control session (a baseline was collected beforehand) with a Polar RS 800CX watch, and throughout the fMRI session with the built-in ECG system of the scanner. Diastolic and systolic blood pressure was recorded directly before and after participants immersed their hand in the water bath. In line with previous reports, blood pressure and pulse did not differ significantly between Stress and Control participants either before or after the SECPT procedure (Schwabe et al., 2008).

Self-report ratings

Immediately after completing the stress/control procedure, participants indicated on a visual analog scale (VAS), their perceived stress level (PSL), how much they felt in control of the situation, and how angry, sad, happy, anxious, and hungry they felt. All rating scales ranged from 0 (“not at all”) to 100 (“extremely”) (see Supplemental Experimental Procedures).

Behavioral analyses

Logistic regression over all choices

We examined the impact of taste and health attributes as well as recommendations on each participant’s choices by computing the following logistic regression:

$$[1] \text{ CL} = \beta_0 + \beta_1 \text{Taste}_L + \beta_2 \text{Taste}_R + \beta_3 \text{Health}_L + \beta_4 \text{Health}_R + \beta_5 \text{ReCL} + \beta_5 \text{ReCR} + \varepsilon$$

In which CL is a binary choice vector taking the value of 1 whenever the left option is selected and 0 otherwise, and the subscripts L and R denote the taste,

health, and recommendation status of the left and right items, respectively. Recommendation regressors took the value of 1 whenever that food was recommended and 0 otherwise. Taste and health ratings for each participant were measured using a visual analog scale and z-scored within participants. Differences in the regression coefficients between the Stress and Control groups were assessed using two sample t-tests.

Logistic regression for self-control failure

We modeled the probability of self-control failure in a generalized linear mixed effects model fit by maximum likelihood (Laplace approximation) as a function of the binary variable Group (Stress, Control), and continuous variables of PSL and cortisol level at the subject level and the difference in health and taste between both items, and the recommendations at the trial level. The model included all one, two, and three way interactions between subject level variables and the three trial level variables (see Table S1A for full the listing). For clarity we present the model with only trial level variables below.

$$[2] \text{ SCF} = \beta_0 + \beta_1 H_{\text{diff}} + \beta_2 T_{\text{diff}} + \beta_3 H_{\text{Rec}} + \varepsilon$$

SCF is a binary vector taking the value of 1 whenever the participant chooses a less healthy, but tastier item (i.e. self-control failure). T_{diff} is the absolute value of the difference in taste ratings between the two foods, and H_{diff} is the absolute value of the difference in health ratings between the two foods. H_{Rec} takes the value of 1 whenever the healthier food is recommended, 0 when there is no recommendation, and -1 when the less healthy food is recommended. The

subject level variables PSL and cortisol were z-scored across participants. Note that repeating the model with rank-transformed AUC cortisol values yields similar results (see Table S1B).

fMRI models

The details of the fMRI data acquisition and preprocessing are given in the Supplemental Experimental Procedures.

For each fMRI analysis, we computed general linear models at the single subject level with the Statistical Parametric Mapping (SPM8, Update Rev. Nr. 5236; Functional Imaging Laboratory, University College London) software suite in Matlab, and examined the results at the second, group level using non-parametric permutation tests (N = 5000 permutations) with threshold-free cluster enhancement (TFCE) as implemented in the Randomise function from the FMRIB Software Library 5.0 (FSL; FMRIB, Oxford) (Hayasaka and Nichols, 2003; Jenkinson et al., 2012). All results are reported family-wise error (FWE) corrected and all coordinates are given in MNI space.

GLM-subjective food value (FV)

To examine neural correlates for the subjective value of the chosen food, we constructed a model with regressors identifying three events of interest (GLM-FV): 1) all choices, 2) trials when the recommended item was chosen, 3) trials when the recommended item was not chosen. Two parametric modulators were included with the first regressor for all choices: P1) the subjective value of the chosen item (FVc), P2) the subjective value of the non-chosen food item (FVnc). Food values for the chosen and non-chosen food were computed as a weighted

addition of the taste and health attributes with the weights derived from the logistic regression over all choices described above in equation [1]. In this and all other fMRI analyses, the regressors were defined as boxcar functions with duration equal to the reaction time on that trial, and regressors for head motion, cardiac, and respiratory effects were included to account for BOLD signal variability associated with these effects.

We computed first level contrasts for: 1) FVc, and 2) FVc-FVnc. Lastly, we calculated one and two sample permutation tests to identify activity for all participants or to compare the Stress and Control groups on each measure, respectively.

GLM-health, taste value (HT)

In GLM-HT, we examined the effects of health, taste, and recommendations on BOLD activity using a model with regressors identifying five events of interest: 1) all choice onsets, 2) trials in which the healthier food was recommended and chosen, 3) trials in which the healthier food was recommended and not chosen, 4) trials in which the less healthy food was recommended and chosen, 5) trials in which the less healthy food was recommended and not chosen. Four parametric modulators were included with the first regressor for all choices: P1) Health rating for chosen item (Hc), P2) Taste rating for chosen item (Tc), P3) Health rating for non-chosen item (Hnc), P4) Taste rating for non-chosen item (Tnc). These parametric regressors were not orthogonalized with respect to one another.

We computed first level contrasts for: 1) Tc, 2) Tnc, 3) Hc, 4) Hnc, 5) Tc-Tnc, and 6) Hc-Hnc. Next, we computed a two-sample permutation test between

the Stress and Control groups comparing the relative taste value ($T_c - T_{nc}$) and relative health value ($H_c - H_{nc}$) signals and covariate permutation tests to identify effects associated with individual differences in PSL and cortisol levels. In the relative taste value analysis, we corrected for multiple comparisons within an anatomically defined ROI encompassing all voxels with a non-zero probability of belonging to the bilateral amygdalae or nucleus accumbens as defined by the Harvard-Oxford subcortical atlas (Desikan et al., 2006).

GLM-override unhealthy recommendation (OR)

The behavioral analyses showed that both Stressed and Control participants were able to override recommendations for the less healthy item that were incongruent with their health goal. Thus, we expanded the original GLM-FV to include five (as opposed to the original 3) events of interest: 1) all choices, 2) trials in which the healthier food was recommended and chosen, 3) trials in which the healthier food was recommended and not chosen, 4) trials in which the less healthy food was recommended and chosen, 5) trials in which the less healthy food was recommended and not chosen. Regressor 1 was parametrically modulated by P1) the subjective value of the chosen food (FV_c), and P2) the subjective value of the non-chosen food (FV_{nc}).

We computed first level contrasts for the difference between choosing the healthier versus the less healthy food following a recommendation for the less healthy food (regressors 5 and 4). Lastly, we calculated one and two sample permutation tests to identify activity for all participants or to compare the Stress and Control groups, respectively.

PPI

In order to investigate whether the effective connectivity of the vmPFC node of the valuation system identified in GLM-FV differed between stressed and control participants during choices in which they selected the tastier item, we ran a psychophysiological interaction analysis (PPI). First, we created a vmPFC timeseries by extracting the first eigenvariate from a 5mm sphere surrounding the subject-specific peak voxel for the parametric effect of FVc from GLM-FV within a functional vmPFC mask defined by all significant voxels in the analysis over all participants at $p = 0.005$ uncorrected. Second, we computed the interaction terms between the vmPFC, and 1) PPI-T, a regressor identifying all trials in which the participant chose the tastier item or 2) PPI-H, a regressor identifying all trials in which the participant chose the healthier item. Third, we estimated a PPI GLM including the following regressors: 1) trials when the healthier item was chosen, 2) trials when the tastier item was chosen, 3) the vmPFC seed time course, 4) PPI-H, and 5) PPI-T.

We computed the first level contrasts for PPI-T and PPI-H minus PPI-T. Lastly, we computed two-sample permutation tests to identify significant differences in these contrasts between the Stress versus Control groups and covariate permutation tests to identify PPI effects associated with individual differences in PSL and cortisol levels.

Author contributions

S.U.M. and T.A.H. designed research; S.U.M. and A.B.M. performed research; S.U.M., A.B.M. and T.A.H. analyzed data; S.U.M. and T.A.H. wrote the manuscript with input from A.B.M.

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Figure legends

Figure 1. Task structure. Participants had 3 seconds to choose one of two food options on each trial, followed by a 2-6 second jittered inter trial interval in which a health reminder symbol was displayed in the center of the screen. In most trials, the food that the participant had previously rated as being the healthier of the two options was highlighted with a white frame. This white frame represented a choice recommendation to the participant. However, participants knew that in some cases the less healthy item could be highlighted (last depicted trial), in which case they should override the misleading recommendation and choose the healthier item.

Figure 2. The stress induction procedure changed individual measures of stress and overall choice behavior. Panel (A) shows that perceived stress levels differ significantly between the Stress and Control groups ($Z = 2.03$, $p = .02$). Each square or circle represents an individual participant in the Stress or Control group, respectively. The horizontal lines indicate the median for each group. Ratings were made on a scale from 0 (“not at all”) to 100 (“extremely”) just after the SECPT or control procedure finished. Panel (B) shows the average salivary cortisol levels for the Stress and Control groups at baseline (stressor offset +1 minute), peak (stressor onset +25 minutes), directly after the choice task (stressor onset +45 minutes), and at the end of the experiment (stressor onset +70 minutes). Participants in the Stress group had significantly greater area under the curve than Controls ($Z = 1.87$, $p = 0.03$). C) The bar graph depicts beta coefficient weights from a logistic regression examining the effects of taste ratings, health ratings, and recommendations for the left and right items on the

probability of selecting the left item. The taste of each food had a stronger impact on choice in the Stress compared to the Control group (TL $t_{49} = 2.13$, $p = 0.04$; TR $t_{49} = -2.30$, $p = 0.03$; also see Table S3). All error bars indicate the standard error of the mean (SEM) across participants.

Figure 3. Stress induced differences in the influence of taste on self-control choice behavior and neural activity. **A)** The error bar plot shows the probability of self-control failure for each group as a function of the difference in taste between the two food items ($|\text{taste left} - \text{taste right}|$). Taste difference values were divided into quintiles to show the increasing probability of self-control failure in the Stress group as taste difference increases (see Tables S1A and S2). **B)** The statistical parametric maps show two regions of the ventral striatum (left) and amygdala (right) where the correlation with relative taste value is higher in the Stress compared to Control group ($p < 0.05$ SVC; see Fig. S1A and Table S5). The color scale represents t-statistics derived from 5000 permutations of the data. **C)** The bar graph shows beta coefficients for relative taste value averaged across all voxels in an anatomical mask of the bilateral nucleus accumbens and amygdala (shown in magenta on the inset brain rendering). The correlation with relative taste value was greater in the Stress compared to the Control group in this anatomically defined ROI ($Z = 2.67$, $p = 0.0069$; see Fig. S1B). All error bars indicate SEM across participants.

Figure 4. Stress induction resulted in greater functional connectivity between the vmPFC and ventral striatum and amygdala when choosing the tastier food. The statistical parametric map shows areas of the ventral striatum (upper) and

amygdala (lower) where the increase in functional connectivity with vmPFC on trials in which the tastier item was chosen is greater for Stress than Control participants ($p < 0.05$ SVC; see Table S6). The color scale represents t-statistics derived from 5000 permutations of the data.

Figure 5. Connectivity between vmPFC and Amyg/vStr and dlPFC are differentially associated with individual differences in PSL and cortisol levels. The brain rendering on the left shows the vmPFC region reflecting the subjective value of food items in red (see Table S4) and regions of the vStr and dlPFC from which the scatter plots in **A-D** are derived in magenta and green, respectively. The magenta voxels in vStr represent the conjunction between voxels showing greater taste choice PPI with vmPFC in the Stress vs Control participants (see Table S6) and those in which taste choice PPI correlates more strongly with cortisol than PSL (see Table S7). The green voxels in dlPFC represent the conjunction between voxels that are more active when using self-control to override taste preferences (see Table S8) and unhealthy recommendations and those in which healthier minus tastier food choice PPI correlates more strongly with PSL than cortisol (see Table S10). Panels **A and B** show scatterplots of dlPFC PPI coefficients with vmPFC for healthier minus tastier food choices against PSL and cortisol levels in green. Panels **C and D** show scatterplots of vStr PPI coefficients with vmPFC for tastier food choices against PSL and cortisol levels in magenta. The black lines in **A-D** indicate robust fits from regressions using iteratively reweighted least squares with a bisquare weighting function.

Supplemental Figures

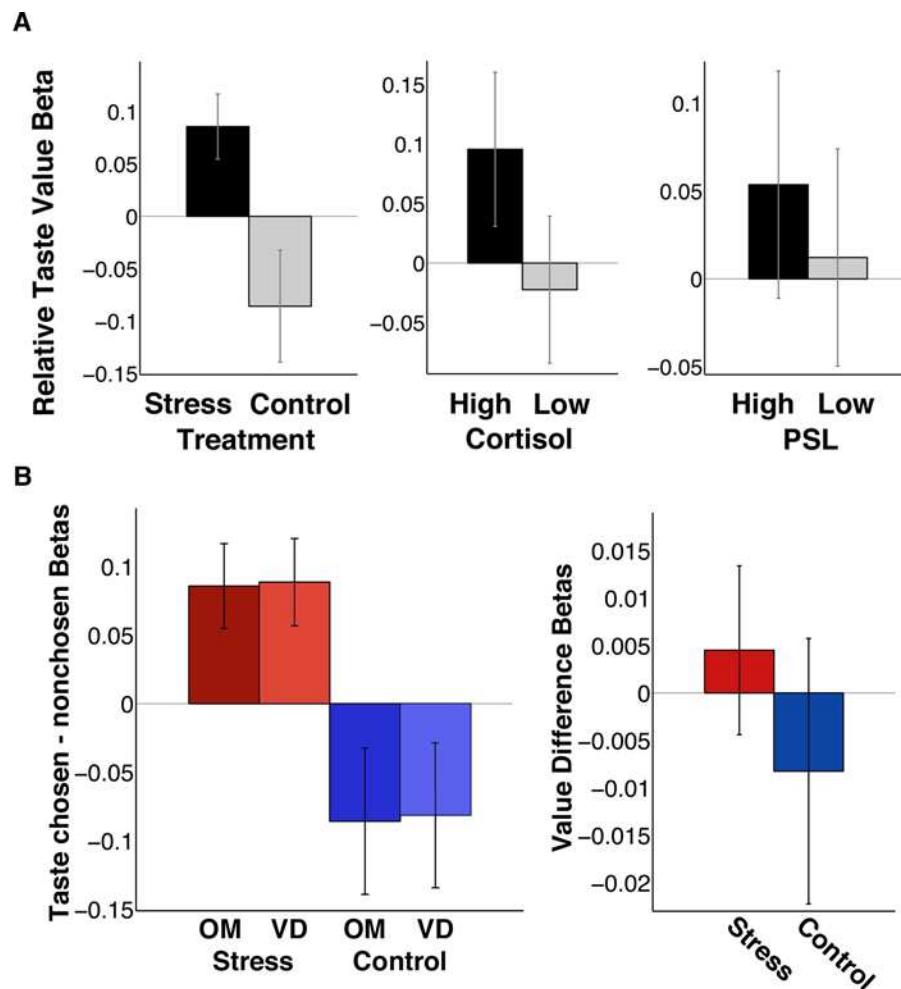


Figure S1, Related to Figure 3. A) Representation of the relative taste value (Taste chosen – nonchosen) in the Amyg/vStr broken down by median splits for cortisol (middle) and Perceived Stress Level (right). For comparison, the left panel shows the relative taste value betas in the Stress and Control groups (Figure 3C in the main text). **B)** The left panel compares the relative taste value betas in the anatomical region of interest that comprises bilateral amygdala and nucleus accumbens from GLM-HT (OM = Original Model) and a version of GLM-HT that additionally accounts for value difference (Value Difference = VD) for both Stress and Control treatment group (see Supplemental Experimental Procedures for GLM-HT-FVdiff). The right panel compares the representation of value difference for both Stress and Control treatment group in the same bilateral amygdala and nucleus accumbens voxels. All error bars denote standard error of the mean (SEM) across participants.

Supplemental Tables

Table S1. Probability of self-control failure by stress treatment group, perceived stress level and cortisol response (Related to Figure 3A).

<i>Regressor</i>	<i>Estimate</i>	<i>Std. Error</i>	<i>z value</i>	<i>p(z)</i>
Intercept	-0.15	0.34	-0.44	0.66
Stress group (S)	0.26	0.44	0.58	0.56
Cortisol (CORT)	-0.09	0.37	-0.24	0.81
Perceived Stress Level (PSL)	-0.14	0.33	-0.42	0.68
H_{diff}	-1.01	0.09	-11.10	< 2e-16
T_{diff}	0.43	0.08	5.75	8e-09
Recommendation (Rec)	-0.54	0.07	-7.40	1e-13
S X CORT	0.23	0.44	0.52	0.61
S X PSL	0.04	0.42	0.09	0.93
CORT X PSL	0.02	0.35	0.05	0.96
S X H _{diff}	0.06	0.12	0.53	0.59
CORT X H _{diff}	0.11	0.09	1.18	0.24
PSL X H_{diff}	0.25	0.09	2.84	0.01
S X T_{diff}	0.42	0.10	4.23	0.00002
CORT X T _{diff}	0.04	0.09	0.46	0.65
PSL X T _{diff}	0.01	0.07	0.12	0.90
S X Rec	-0.14	0.10	-1.50	0.13
CORT X Rec	0.18	0.08	2.31	0.02
PSL X Rec	0.18	0.07	2.47	0.01
S X CORT X PSL	-0.11	0.42	-0.27	0.79
S X CORT X H _{diff}	-0.20	0.11	-1.85	0.07
S X PSL X H _{diff}	-0.17	0.11	-1.54	0.12
CORT X PSL X H _{diff}	0.08	0.08	0.96	0.34
S X CORT X T _{diff}	-0.14	0.10	-1.36	0.17
S X PSL X T_{diff}	0.24	0.10	2.40	0.02
CORT X PSL X T_{diff}	0.18	0.08	2.19	0.03
S X CORT X Rec	-0.22	0.09	-2.34	0.02
S X PSL X Rec	-0.17	0.09	-1.80	0.07
CORT X PSL X Rec	0.02	0.07	0.27	0.79
S X CORT X PSL X H _{diff}	-0.07	0.10	-0.69	0.49
S X CORT X PSL X T_{diff}	-0.20	0.10	-1.93	0.05
S X CORT X PSL X Rec	-0.10	0.09	-1.12	0.26

Estimates are logistic regression coefficients from a mixed-effects generalized linear model fit by maximum likelihood.

H_{diff} is the absolute health difference between both items; T_{diff} is analogously the absolute taste difference between both items.

Recommendation was modeled with the value of 1 for a healthy recommendation, 0 for no recommendation, and -1 for an unhealthy recommendation.

Stress group was modeled as a binary factor taking the value of 1 for participants in the Stress group and 0 for controls.

Perceived stress levels were measured using a visual analog scale and normalized (z-scored) across participants.

Cortisol response was calculated as the Area Under the Curve with respect to ground after (Pruessner et al., 2003) over the course of the whole study session (from minute +1 to minute +70) and normalized (z-scored) across participants.

Table S2. Probability of self-control failure by stress treatment group, perceived stress level and rank transformed cortisol* response (Related to Figure 3A).

<i>Regressor</i>	<i>Estimate</i>	<i>Std. Error</i>	<i>z value</i>	<i>p(z)</i>
Intercept	-0.15	0.35	-0.43	0.67
Stress group (S)	0.22	0.44	0.50	0.62
Ranked Cortisol (RCORT)	-0.12	0.38	-0.33	0.74
Perceived Stress Level (PSL)	-0.12	0.34	-0.35	0.73
H_{diff}	-1.01	0.09	-11.05	< 2e-16
T_{diff}	0.43	0.07	5.79	7e-09
Recommendation (Rec)	-0.55	0.07	-7.41	1e-13
S X RCORT	0.28	0.45	0.62	0.54
S X PSL	0.02	0.43	0.05	0.96
RCORT X PSL	0.00	0.40	0.00	1.00
S X H _{diff}	0.05	0.12	0.44	0.66
RCORT X H _{diff}	0.10	0.09	1.05	0.29
PSL X H_{diff}	0.25	0.09	2.84	0.005
S X T_{diff}	0.41	0.10	4.07	0.00005
RCORT X T _{diff}	0.03	0.09	0.33	0.74
PSL X T _{diff}	0.01	0.07	0.19	0.85
S X Rec	-0.13	0.09	-1.36	0.17
RCORT X Rec	0.19	0.08	2.40	0.02
PSL X Rec	0.17	0.07	2.33	0.02
S X RCORT X PSL	-0.08	0.46	-0.17	0.86
S X RCORT X H _{diff}	-0.20	0.11	-1.78	0.07
S X PSL X H _{diff}	-0.16	0.11	-1.48	0.14
RCORT X PSL X H _{diff}	0.08	0.09	0.91	0.36
S X RCORT X T _{diff}	-0.16	0.11	-1.50	0.13
S X PSL X T_{diff}	0.24	0.10	2.40	0.02
RCORT X PSL X T _{diff}	0.15	0.09	1.69	0.09
S X RCORT X Rec	-0.22	0.09	-2.38	0.02
S X PSL X Rec	-0.16	0.09	-1.78	0.08
RCORT X PSL X Rec.	0.05	0.08	0.58	0.56
S X RCORT X PSL X H _{diff}	-0.09	0.11	-0.82	0.41
S X RCORT X PSL X T _{diff}	-0.15	0.11	-1.31	0.19
S X RCORT X PSL X Rec.	-0.14	0.10	-1.50	0.13

*This additional replication of the regression in Table S1 above was run to test whether the distribution of the non-linear cortisol AUC measure had a strong impact on the regression coefficients. The results indicate that this was not the case.

Cortisol response was calculated as the Area Under the Curve with respect to ground after (Pruessner et al., 2003) over the course of the whole study session (from minute +1 to minute +70) and then rank transformed across participants.

All other details are identical to Table S1.

Table S3. Probability of self-control failure by stress treatment group, perceived stress level and cortisol response *controlling for hunger level* (Related to Figure 3A).

<i>Regressor</i>	<i>Estimate</i>	<i>Std. Error</i>	<i>z value</i>	<i>p(z)</i>
Intercept	-0.07	0.37	-0.19	0.85
Stress group (S)	0.11	0.47	0.24	0.81
Cortisol (CORT)	-0.07	0.36	-0.20	0.84
Perceived Stress Level (PSL)	-0.23	0.37	-0.62	0.54
H_{diff}	-1.01	0.09	-11.08	< 2e-16
T_{diff}	0.43	0.07	5.74	9e-09
Recommendation (Rec)	-0.54	0.07	-7.39	1e-13
<i>Hunger level</i>	-0.30	0.54	-0.55	0.58
S X CORT	0.21	0.44	0.49	0.63
S X PSL	0.08	0.45	0.18	0.86
CORT X PSL	0.07	0.36	0.18	0.85
S X H _{diff}	0.06	0.12	0.52	0.60
CORT X H _{diff}	0.11	0.09	1.19	0.23
PSL X H_{diff}	0.25	0.09	2.84	0.005
S X T_{diff}	0.42	0.10	4.23	0.00002
CORT X T _{diff}	0.04	0.09	0.46	0.64
PSL X T _{diff}	0.01	0.07	0.11	0.91
S X Rec	-0.14	0.09	-1.50	0.13
CORT X Rec	0.18	0.08	2.31	0.02
PSL X Rec	0.18	0.07	2.47	0.01
<i>S X Hunger level</i>	0.10	0.58	0.17	0.86
S X CORT X PSL	-0.11	0.43	-0.26	0.80
S X CORT X H _{diff}	-0.20	0.11	-1.85	0.07
S X PSL X H _{diff}	-0.17	0.11	-1.55	0.12
CORT X PSL X H _{diff}	0.08	0.08	0.96	0.34
S X CORT X T _{diff}	-0.14	0.10	-1.36	0.17
S X PSL X T_{diff}	0.24	0.10	2.41	0.02
CORT X PSL X T_{diff}	0.18	0.08	2.20	0.03
S X CORT X Rec	-0.22	0.09	-2.33	0.02
S X PSL X Rec	-0.17	0.09	-1.81	0.07
CORT X PSL X Rec	0.02	0.07	0.27	0.79
S X CORT X PSL X H _{diff}	-0.07	0.10	-0.68	0.50
S X CORT X PSL X T_{diff}	-0.20	0.10	-1.93	0.05
S X CORT X PSL X Rec	-0.10	0.09	-1.12	0.26

This additional replication of the regression in Table S1 above was run to test whether hunger level had an impact on self-control choices. The results indicate that this was not the case.

Hunger levels were measured using a visual analog scale and normalized (z-scored) across participants.

All other details are identical to Table S1.

Table S4. The influence of stress on choice reaction times (Related to Figure 3).

<i>Regressor</i>	<i>Estimate</i>	<i>Std. Error</i>	<i>t value</i>	<i>p(z)</i>
Intercept	0.425	0.044	9.765	1e-12
Stress group (S)	-0.021	0.056	-0.374	0.710
Perceived Stress Level (PSL)	0.014	0.044	0.324	0.748
Cortisol (CORT)	-0.029	0.047	-0.622	0.537
T _{diff}	-0.011	0.006	-1.889	0.059
H_{diff}	-0.100	0.006	-17.104	< 2e-16
Recommendation (Rec)	-0.032	0.005	-5.858	5e-09
MHLT	0.033	0.011	3.031	0.002
LHMT	0.059	0.014	4.202	0.00003
S X PSL	-0.026	0.055	-0.480	0.634
S X CORT	0.047	0.057	0.830	0.411
PSL X CORT	-0.008	0.047	-0.166	0.869
S X T_{diff}	-0.018	0.007	-2.438	0.015
PSL X T _{diff}	-0.002	0.006	-0.441	0.659
CORT X T_{diff}	-0.012	0.006	-1.951	0.051
S X H_{diff}	0.018	0.008	2.452	0.014
PSL X H_{diff}	0.012	0.006	1.977	0.048
CORT X H _{diff}	0.000	0.006	-0.014	0.989
S X Rec	0.002	0.007	0.242	0.808
PSL X Rec	0.005	0.006	0.838	0.402
CORT X Rec	0.001	0.006	0.132	0.895
S X MHLT	0.033	0.015	2.302	0.021
PSL X MHLT	-0.014	0.011	-1.248	0.212
CORT X MHLT	-0.019	0.014	-1.371	0.171
S X LHMT	0.006	0.017	0.339	0.735
PSL X LHMT	-0.012	0.014	-0.839	0.402
CORT X LHMT	-0.014	0.013	-1.076	0.282
S X PSL X CORT	-0.061	0.055	-1.113	0.272
S X PSL X T_{diff}	-0.020	0.007	-2.750	0.006
S X CORT X T _{diff}	0.014	0.008	1.824	0.068
PSL X CORT X T _{diff}	-0.022	0.006	-3.551	0.0004
S X PSL X H _{diff}	0.006	0.007	0.856	0.392
S X CORT X H _{diff}	-0.008	0.008	-1.035	0.301
PSL X CORT X H _{diff}	0.005	0.006	0.843	0.399
S X PSL X Rec	-0.002	0.007	-0.336	0.737
S X CORT X Rec	-0.004	0.007	-0.500	0.617
PSL X CORT X Rec	0.009	0.006	1.456	0.145
S X PSL X MHLT	0.047	0.015	3.123	0.002
S X CORT X MHLT	0.010	0.016	0.622	0.534

PSL X CORT X MHLT	-0.024	0.015	-1.644	0.100
S X PSL X LHMT	0.032	0.017	1.919	0.055
S X CORT X LHMT	0.018	0.017	1.085	0.278
PSL X CORT X LHMT	-0.021	0.013	-1.579	0.114
S X PSL X CORT X T_{diff}	0.033	0.007	4.538	0.000006
S X PSL X CORT X H _{diff}	0.002	0.007	0.208	0.836
S X PSL X CORT X Rec	-0.007	0.007	-0.980	0.327
S X PSL X CORT X MHLT	0.013	0.017	0.795	0.427
S X PSL X CORT X LHMT	0.022	0.016	1.383	0.167

Estimates are regression coefficients from a mixed-effects generalized linear model fit by restricted maximum likelihood. P-values for t-tests on regression coefficients use the Satterthwaite approximation to degrees of freedom.

H_{diff} is the absolute health difference between both items; T_{diff} is analogously the absolute taste difference between both items.

Recommendation was modeled with the value of 1 for a healthy recommendation, 0 for no recommendation, and -1 for an unhealthy recommendation.

Choose Healthier & Less Tasty (MHLT; self control success) and choose Tastier & Less Healthy (LHMT; self-control failure) were modeled as a binary factor taking the value of 1 whenever such a choice occurred, and 0 otherwise.

Stress group was modeled as a binary factor taking the value of 1 for participants in the Stress group and 0 for controls.

Perceived stress levels were measured using a visual analog scale and normalized (z-scored) across participants.

Cortisol response was calculated as the Area Under the Curve with respect to ground after (Pruessner et al., 2003) over the course of the whole study session (from minute +1 to minute +70) and normalized (z-scored) across participants.

Table S5. This table represents the results of an additional control analysis examining the probability of choosing the left item in trials with no self-control challenge (i.e. tastier food = healthier food). (Related to Figure 2C).

<i>Regressor</i>	<i>Estimate</i>	<i>Std. Error</i>	<i>z value</i>	<i>p(z)</i>
Intercept	0.14	0.17	0.83	0.41
Stress group (S)	-0.14	0.22	-0.61	0.54
Taste left item	0.61	0.08	7.25	4e-13
Taste right item	-0.56	0.08	-6.65	3e-11
Health left item	1.26	0.10	12.98	< 2e-16
Health right item	-1.28	0.10	-13.37	< 2e-16
Recommendation left item	0.64	0.20	3.25	0.001
Recommendation right item	-0.67	0.20	-3.41	0.0006
Stress X Taste left	0.29	0.12	2.45	0.01
Stress X Taste right	-0.21	0.12	-1.85	0.06
Stress X Health left	-0.29	0.13	-2.26	0.02
Stress X Health right	0.23	0.13	1.80	0.07
Stress X Recommend left	-0.11	0.26	-0.43	0.66
Stress X Recommend right	-0.07	0.26	-0.27	0.79

Because the healthier food is also the tastier food in these cases, there is no need to inhibit button press responses indicating a choice for the tastier food in these trials. The significant Stress X Taste and Stress X Health interactions in this regression and the reaction time results summarized in Table S2 indicate that the stress induction procedure changes the impact of taste and health attributes on choice in a manner that goes beyond simply impairing response inhibition mechanisms.

Estimates are logistic regression coefficients from a mixed-effects generalized linear model fit by maximum likelihood.

Taste and health coefficients denote the normalized (z-scored) taste and health rating for the item presented on the screen (left and right).

Recommendation left was modeled as a binary factor taking the value of 1 when the item on the left side of the screen was recommended 0 otherwise. Recommendation right is the analogous binary regressor for trials in which the item on the right side of the screen was recommended.

Stress group was modeled as a binary factor taking the value of 1 for participants in the Stress treatment group and 0 for the Control treatment group.

Table S6. Regions showing a positive correlation with the subjective value of the chosen food item and the difference between chosen and non-chosen items across participants in both groups (Related to the 3D rendering in Figure 5).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>	<i>TFCE t-stat</i>
<i>Chosen food value</i>			
Cuneus	R	3 -85 15	8.09
Posterior Middle Temporal Gyrus	L	-60 -40 -10	6.97
Inferior Lateral Occipital Cortex	R	55 -70 -7	6.36
vmPFC: Medial Orbitofrontal cortex	L	-5 61 -0	6.2
Planum Temporale	L	-62 -20 9	6.15
Angular Gyrus	R	53 -57 15	6.09
Occipital Pole	L	-10 -95 28	6.03
Inferior Temporal Gyrus	R	73 -32 -19	5.97
Precuneus	L	-5 -82 43	5.84
Lingual Gyrus	R	16 -52 -4	5.83
Middle Temporal Gyrus	R	68 -47 -4	5.67
Frontal Medial Cortex	R	1 46 -19	5.67
Amygdala	L	-27 -5 -10	5.61
Lateral Occipital cortex	L	-52 -67 15	5.5
Precentral Gyrus	L	-15 -27 77	5.42
Brain Stem	L	-15 -25 -28	5.38
Frontal Pole	L	-17 56 37	5.35
vmPFC: Rostral Anterior Cingulate Gyrus	L	-10 38 3	5.3
Middle Temporal Gyrus	R	63 -2 -22	5.22
Precuneus	R	1 -70 59	5.2
Postcentral Gyrus	R	23 -27 59	4.84
Frontal Orbital Cortex	L	-20 18 -25	3.23
Left Hippocampus	L	-20 -15 -19	3.48
Inferior Frontal Gyrus, Pars Triangularis	L	-55 26 12	3.5
Middle Frontal Gyrus	L	-42 -2 65	4.24
Inferior Frontal Gyrus, Pars Opercularis	R	63 26 3	3.9
<i>Chosen minus Nonchosen food value</i>			
Posterior Middle Temporal Gyrus	L	-60 -40 -7	6.51
Central Opercular Cortex	L	-62 -22 15	6.45
Posterior Superior Temporal Gyrus	R	66 -25 21	6.42
Putamen	L	-30 -17 3	6.35
Temporooccipital Middle Temporal Gyrus	R	63 -52 -4	6.35
Temporooccipital Middle Temporal Gyrus	L	-50 -62 9	6.27
Temporooccipital Inferior Temporal Gyrus	R	41 -45 -7	6.22
Occipital Fusiform Gyrus	R	31 -65 -22	5.87
Middle Temporal Gyrus	R	71 -20 -10	5.73

Planum Polare	R	56	-2	3	5.67
Putamen	R	28	-2	3	5.64
Amygdala	L	-22	-2	-10	5.56
Temporal Occipital Fusiform Cortex	L	-47	-62	-25	5.56
Brain Stem	R	13	-35	-19	5.53
Anterior Middle Temporal Gyrus	L	-57	3	-19	5.51
Precentral Gyrus	L	-60	-2	6	5.49
Precentral Gyrus	R	21	-25	59	5.43
Postcentral Gyrus	L	-17	-37	80	5.42
Cuneus	R	1	-85	28	5.42
Middle Temporal Gyrus	L	-70	-17	-7	5.29
Angular Gyrus	R	53	-45	59	2.69
Lateral Occipital Cortex	R	46	-82	-22	2.94
Frontal Pole	L	-20	58	37	3.81
Occipital Pole	R	18	-95	12	2.6
Temporal Pole	L	-17	16	-38	2.42
Precentral Gyrus	L	-7	-17	68	2.56
Postcentral Gyrus	L	-40	-17	37	2.19

All reported regions were significant at $p < .05$ after whole brain family-wise error correction. Threshold free cluster enhancement (TFCE) test statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm with a maximum of 20 sub-peaks per cluster. Anatomical labels were derived from the Automated Anatomical Labeling (AAL (Tzourio-Mazoyer et al., 2002)) and Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

Table S7. Regions showing stronger correlations with relative taste value in the Stress versus Control group (Related to Figure 3B).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>	<i>TFCE t-stat</i>
Hippocampus / Amygdala	L	-27 -10 -22	4.95
Amygdala	R	13 -10 -13	4.25
Nucleus accumbens	R	6 11 -7	4.41
Amygdala	R	26 1 -19	3.77

Results represent the peak coordinates for the contrast of Tc minus Tnc from GLM-HT. The reported regions were significant at $p < .05$ after family-wise error correction in a region of interest composed of bilateral Nucleus accumbens and Amygdala. Threshold free cluster enhancement (TFCE) test statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm with a maximum of 20 sub-peaks per cluster. Anatomical labels were derived from the Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

Table S8. Regions showing stronger coupling with vmPFC during tastier choices in Stress compared to Control participants (Related to Figure 4).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>	<i>TFCE t-stat</i>
Central Opercular Cortex	L	-45 -5 6	4.57
Heschl's Gyrus / Insular Cortex	L	-35 -25 15	3.23
Temporal Pole	L	-30 6 -38	3.93
Anterior Parahippocampal Gyrus	L	-22 -12 -28	3.75
Precentral Gyrus	R	46 -10 49	4.67
Planum Temporale	R	61 -22 9	4.07
Central Opercular Cortex / Insular Cortex	R	38 -15 18	4.81
Posterior Temporal Fusiform Cortex	L	-40 -15 -28	4
Superior Temporal Gyrus	L	-62 -2 0	3.82
Central Opercular Cortex	R	43 3 12	4.05
Frontal Orbital Cortex	L	-22 8 -10	4.44
White Matter (near Precentral Gyrus)	L	-27 -22 34	5.1
Temporal Pole	R	58 8 -7	4.49
Planum Temporale / Superior Temporal Gyrus	L	-65 -20 9	3.89
Central Opercular Cortex / Heschl's Gyrus	R	53 -12 9	4.14
Putamen / Nucleus accumbens*	L	-15 13 -13	4.05
Superior Temporal Gyrus	L	-52 -10 -10	4.96
Temporal Pole	L	-42 18 -25	4.61
Inferior Frontal Gyrus, pars opercularis	L	-40 -15 18	3.51
Amygdala*	L	-22 -2 -22	3.82
Hippocampus	L	-30 -10 -22	3.55

Results represent the peak coordinates for the tastier choice PPI. All reported regions were significant at $p < .05$ after whole brain family-wise error correction. The regions of amygdala and putamen/nucleus accumbens marked with asterisks are also the peaks for a small volume correction conducted within a region of interest composed of bilateral Nucleus accumbens and Amygdala. Threshold free cluster enhancement (TFCE) test statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm with a maximum of 20 sub-peaks per cluster. Anatomical labels were derived from the Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

Table S9. Regions in which vmPFC PPI during tastier food choices is more strongly correlated with cortisol than perceived stress level (Related to Figure 5).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>	<i>TFCE t-stat</i>
Putamen	L	-22 -2 6	4.64
Inferior Frontal Gyrus pars triangularis	L	-47 31 6	4.46
Middle Frontal Gyrus	L	-37 8 37	4.31
Middle Frontal Gyrus	L	-42 31 28	4.26
Postcentral Gyrus	L	-62 -15 28	4.12
Thalamus	L	-25 -22 15	4.11
Postcentral Gyrus	L	-30 -35 49	4.04
Inferior Frontal Gyrus p. operc./ Precentral Gyrus	L	-52 8 18	3.79
Superior Lateral Occipital Cortex	L	-32 -60 40	3.62
Frontal Pole	L	-42 51 18	3.49
Frontal Pole	L	-27 46 31	3.42
Postcentral Gyrus / Superior Parietal Lobule	L	-47 -40 59	3.35
Precentral Gyrus / Postcentral Gyrus	L	-37 -12 37	3.31
Insular Cortex	L	-37 16 -4	3.3
Insular Cortex	L	-42 -5 6	3.28
Anterior Superior Temporal Gyrus	L	-60 -2 -7	3.26
Superior Lateral Occipital Cortex	L	-17 -67 55	3.03
Intracalcarine Cortex / Lingual Gyrus	R	8 -85 0	4.77
Lingual Gyrus	L	-17 -55 0	4.53
Temporooccipital Inferor Temporal Gyrus	R	48 -55 -7	4.5
Lingual Gyrus / Occipital Fusiform Gyrus	L	-17 -72 -13	4.48
Brain Stem	L	-5 -32 -7	4.19
Cerebellum (Culmen)	R	31 -45 -31	4.17
Intracalcarine Cortex / Superior Lateral Occipital Cortex	L	-17 -85 12	4.1
Lingual Gyrus	R	16 -60 -16	4.06
Superior Lateral Occipital Cortex	L	-32 -80 24	3.99
Temporal Occipital Fusiform Cortex	L	-40 -47 -28	3.61
Brain Stem	R	13 -32 -22	3.15
Occipital Pole	L	-17 -92 31	3.01
Temporooccip. Inf. Temp. Gyrus / Middle Temporal Gyrus	L	-52 -60 -7	2.99
Intracalcarine Cortex / Lingual Gyrus	R	31 -60 3	2.67
Occipital Pole	R	18 -97 12	2.59
Occipital Pole	L	-7 -95 -10	2.54
Occipital Fusiform Gyrus	R	33 -70 -22	2.38
Cerebellum (Culmen)	L	-10 -50 -19	2.31
Posterior Superior Temporal Gyrus / Supramarginal Gyrus	R	51 -35 9	4.51
Superior Frontal Gyrus	L	-15 -2 71	4.1

Precuneous Cortex	R	1 -57 56	4.46
Postcentral Gyrus	R	63 -7 24	4.06
Postcentral Gyrus	R	28 -32 71	4.24
Superior Parietal Lobule / Angular Gyrus	R	33 -50 46	3.92
Precentral Gyrus	R	13 -27 62	3.73
Postcentral Gyrus	L	-20 -40 59	3.43
Temporooccipital Inferor Temporal Gyrus	L	-50 -47 -10	4
Superior Lateral Occipital Cortex	R	28 -62 31	4.53
Middle Frontal Gyrus	R	31 8 43	4.91
Precentral Gyrus	L	-2 -17 59	3.33
Posterior Supramarginal Gyrus	R	33 -37 40	3.35
Right Caudate	R	18 21 6	3.95
Superior Lateral Occipital Cortex	R	26 -60 49	3.41
Superior Frontal Gyrus	L	-2 31 46	3.44
Postcentral Gyrus	R	36 -32 62	3.08
Postcentral Gyrus / Precuneous Cortex	R	13 -40 55	3.52
Posterior Cingulate Gyrus	L	-2 -17 46	3.33
Cerebellum (Culmen / Vermis)	L	-2 -60 -13	3.87
Precuneous Cortex	L	-5 -45 46	3.83
Inferior Lateral Occipital Cortex	R	31 -80 6	3.94
Occipital Pole	L	-5 -97 3	3.73
Superior Parietal Lobule	L	-17 -57 59	3.86
Anterior Cingulate Gyrus	L	-5 16 31	3.28
Precuneous Cortex / Postcentral Gyrus	R	16 -35 46	3.41
Anterior Cingulate Gyrus	L	-5 18 37	3.83
Temporooccipital Middle Temporal Gyrus	R	53 -50 0	2.33

Results represent the peak coordinates for the tastier choice PPI. All reported regions were significant at $p < .05$ after whole brain family-wise error correction. Threshold free cluster enhancement (TFCE) test statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm with a maximum of 20 sub-peaks per cluster. Anatomical labels were derived from the Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

Table S10. Regions showing greater activity for self-control choices (Related to the 3D rendering in Figure 5).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>	<i>TFCE t-stat</i>
Middle/Inferior Frontal Gyrus	L	-45 16 31	5.3
Frontal Pole/Superior Frontal Gyrus	L	-20 56 34	5.86
Superior Parietal Lobule	L	-27 -67 55	5.61
Paracingulate/Anterior Cingulate Gyrus	L	-2 33 31	4.25
Paracingulate/Superior Frontal Gyrus	R	1 36 40	3.96
Frontal Pole/Superior Frontal Gyrus	L	-20 53 21	3.87

All reported regions were significant at $p < .05$ after whole brain family-wise error correction. Threshold free cluster enhancement (TFCE) test statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm with a maximum of 20 sub-peaks per cluster. Anatomical labels were derived from the Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

This table is included for the facilitation of future experiments and meta-analyses. It reports uncorrected p-values that are not used as the basis for any inferences made in the current work.

Table S11. Regions showing greater activity for the contrast Unhealthy minus Healthy recommendation trials in the Stress versus Control participants (not related to any main text or figures).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>			<i>T-stat</i>
Superior Frontal Gyrus	R	6	23	59	4.56
Inferior Frontal Gyrus, pars opercularis	L	-57	16	6	3.66
Superior Frontal Gyrus	L	-5	16	62	3.72
Frontal Pole	L	-27	41	37	3.81
Frontal Pole	L	-37	56	18	3.43
Superior Frontal Gyrus	R	23	11	49	3.66
Middle Frontal Gyrus	R	48	6	46	3.8
Paracingulate Gyrus	R	11	11	46	3.71
Precuneous Cortex	L	-25	-52	24	3.47
Frontal Orbital Cortex	L	-25	16	-19	3.41
Temporal Pole	L	-50	11	-19	3.24

All reported regions were significant at the $p < .001$ uncorrected level and contain at least 3 voxels. T statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm. Anatomical labels were derived from the Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

Table S12. Regions in which the difference in vmPFC PPI for healthier versus tastier food choices is more strongly correlated with perceived stress level than cortisol (Related to Figure 5).

<i>Region</i>	<i>Side</i>	<i>MNI Coordinates</i>	<i>TFCE t-stat</i>
Occipital Fusiform Gyrus	L	-22 -75 -10	4.51
Intracalcarine Cortex	L	-7 -82 3	4.12
Occipital Fusiform Gyrus / Lingual Gyrus	R	13 -82 -13	4.15
Inferior Frontal Gyrus	L	-37 8 24	4.36
Insular Cortex	L	-30 11 6	4.72
Middle Frontal Gyrus	L	-45 31 31	3.96
Frontal Pole	L	-32 41 24	4.34
Lingual Gyrus	R	6 -72 -4	3.51

All reported regions were significant at $p < .05$ after whole brain family-wise error correction. Threshold free cluster enhancement (TFCE) test statistics were calculated with the permutation method described by (Smith and Nichols, 2009) and implemented in FSL. Sub-peaks within clusters formed by contiguous voxels are reported when separated by a distance of 20mm with a maximum of 20 sub-peaks per cluster. Anatomical labels were derived from the Harvard-Oxford cortical and subcortical atlases (Desikan et al., 2006).

Supplemental Experimental Procedures

Participants

The inclusion/exclusion criteria for participants were as follows: All participants had normal or corrected-to-normal vision, were right-handed, non-smokers and refrained from taking any medication for 3 days prior to their scanning session. Individuals taking any prescription medications were excluded from participation. Participants reported no history of somatic or psychiatric disease or drug abuse. In addition, they had no history of eating disorders or food allergies and intolerances, and did not currently follow a specific diet (e.g. vegan, vegetarian, gluten-free, etc.). The mean BMI of all participants included in the fMRI study was 22.55 (\pm 2.06 SD). To ensure a normal reaction of the hypothalamic-pituitary-adrenal (HPA) axis, individuals who reported any history of atopic reactions (including hay fever, dermatitis, and any other allergies) were excluded from participation. To control for HPA axis reaction, participants also did not consume alcohol or caffeine in the 18 hours before the experiment, were instructed to get sufficient sleep in the night before the experiment, and refrained from exercise in the 6 hours before they came to the laboratory. They were instructed to eat a light meal (sandwich or salad) 3 hours before their appointment, and to consume nothing but water until the experiment was over. None of our volunteers had participated in a stress experiment previously (Schommer et al., 2003).

The recruitment and inclusion criteria for this study included a general desire to eat healthy and exercise, while still enjoying the consumption of junk food items. These criteria selected for individuals who would face a self-control challenge in our task. The participants' self-reported typical eating behavior indicates that our request for the participants to "choose the healthier option whenever possible" in this study is consistent with their general efforts to maintain a healthy lifestyle (see Experimental Procedures). Furthermore, we found a significant positive correlation between self-control success in our task and the restrictive eating subscale of the Three Factor Eating Questionnaire ($r = 0.30$, $p = 0.03$). Note that restrictive eating habits did not differ between Stress (median restriction score = 5 ± 1.93 MAD) and Control treatment groups (median restriction score = 6.5 ± 2.59 MAD; $z = -0.88$, $p = 0.38$).

Data of three participants had to be excluded from a subset of analyses. The swab for the baseline cortisol measurement of one participant did not contain enough saliva for analysis and was

coded as missing. This participant was excluded from all analyses that involved comparison to baseline cortisol or cortisol AUC. One participant was an outlier with regard to the peak cortisol measurement and therefore was left out of any behavioral or brain analyses that involved correlations with cortisol. Omitting this outlier from comparisons of means across the treatment groups did not change the results, however. A third participant failed to complete the VAS rating for perceived stress. This participant was excluded from all analyses that involved the perceived stress level.

We restricted our sample in this initial study to men in order to establish changes in the value computation / self-control circuits in a sample of participants with a relatively homogeneous level of gonadal hormones. Sex steroids are known to modulate measures of the neuroendocrine stress response. The salivary free-cortisol response to psychosocial stress in women varies with the stage of the ovulatory cycle (pre- or post-luteal phase) as well as the use of hormonal contraception (Kirschbaum 1999, 1992). For additional details see (Hellhammer et al., 2009). In practice, ensuring the comparability between salivary cortisol measures from women and men is often achieved by testing women who are not using hormonal contraception and are in the post-luteal phase of their cycle. However, the most thorough test of the differential effect of psychosocial stress on self-control in women would require testing the same individual in both her pre- and post-ovulation phases to account for changing levels in gonadal hormones, and given the wide use of hormonal contraceptives in the population, should also include a systematic comparison of the effects of hormonal contraception use. These will be important experiments to conduct in the future.

Choice task

The position of the healthier item and the healthier recommendation were fully randomized to avoid systematic bias toward one side of the screen. The allocation of trials into recommendation conditions was also random. Choice pairs were created according to the individual participants' health and taste ratings. Our matching algorithm ensured that only foods with unequal health ratings were paired in order to make sure that we could classify our recommendations as correct (i.e. for the healthier item) or incorrect. Trials with correct, incorrect, or no recommendation were then allocated equally across the three runs, such that each run contained 40 trials with a correct recommendation, 20 trials with an incorrect recommendation, and 10 trials without a recommendation. These trial types were presented in a completely randomized order within each run.

Cortisol analysis

Salivary cortisol was analyzed by the laboratory of Prof. Clemens Kirschbaum (TU Dresden, Germany) using a commercially available competitive luminescence immunoassay (CLIA; IBL, Hamburg, Germany). The intra- and interassay coefficients of variation for cortisol were below 8%. Salivary cortisol concentrations are reported in nanomol/liter. A Kolmogorov-Smirnov-Test revealed that cortisol values were not normally distributed within the Stress group and thus statistical comparisons using cortisol values were performed with non-parametric tests. Five participants in the Stress group took their hand out of the water bath before the undisclosed 3-minute duration of the SECPT was over. When this occurred, according to the SECPT test protocol, the participants were instructed to try putting their hand back in the water if they could, and to remain still and look into the camera until the test was over. Three of the five re-inserted their hand in the cold water bath several times. In total, the five participants endured the water bath for a mean duration of 103 seconds (SD = 43 s).

The level of salivary cortisol (calculated as Area Under the Curve with respect to ground over the total time of the session after (Pruessner et al., 2003)) did not differ between participants who removed their hand (mean = 430, SD = 287) and those who did not (mean = 550, SD = 265) (Wilcoxon rank sum test $Z = -1.16$, $p = 0.25$). However, these individuals did have higher self-reported stress levels (PSL) (Wilcoxon rank sum test $Z = 2.25$, $p = 0.02$). We believe that the most likely reason for the high PSL ratings in participants who removed their hand early was a sense of failure. The participants were explicitly told that they were being evaluated during the SECPT. Removing the hand before instructed to do so meant implicitly admitting that they could not tolerate the cold water and would be evaluated negatively by the opposite sex experimenter observing them. Excluding the 5 participants who withdrew their hand early does not change any of the relationships between stress induction, PSL, or cortisol and behavior and therefore these participants were included in all analyses.

Psychometric inventories

After the fMRI scan, participants completed German versions of the Three Factor Eating Questionnaire (Pudel and Westenhöfer, 1989), the Spielberger State-Trait Anxiety Inventory (Laux et al., 1981), and the Behavioral Inhibition and Activation Scales (Strobel et al., 2001).

Self-report ratings

A Kolmogorov-Smirnov-Test revealed that values for the perceived stress level (PSL) were not normally distributed. For this reason and for consistency with the group level fMRI analyses, statistical comparisons between Stress and Control group with regard to perceived stress level were performed with non-parametric permutation tests.

Health, taste, and appetitiveness ratings

Participants used a continuous rating scale, on which anchor points were depicted in steps of 1 (range from -5 for “very untasty / unhealthy” to +5 for “very tasty / healthy”). For clarity, we report ratings as % of maximum taste or health scale value. Median taste and health ratings in the Stress and Control groups did not differ (taste Stress = 56.10%, taste Controls = 54.22%; $Z = -0.81$, $p = .42$; health Stress = 47.42%, health Controls = 44.84%; $Z = -0.81$, $p = .42$). The median correlation between health and taste ratings was -0.09 ± 0.31 MAD in the Stress group, and -0.06 ± 0.20 MAD in the Control group. Appetitiveness ratings also did not differ between the two groups ($Z = -0.23$, $p = 0.81$).

Lastly, health ($r = -0.12$, $p = 0.40$), taste ($r = 0.09$, $p = 0.56$), and appetitiveness ratings ($r = 0.13$, $p = 0.37$) were not correlated with hunger levels. For these correlations, the Pearson correlation coefficients (r) were tested against a null distribution generated from 5000 permutations of the data to compute two-tailed p-values.

Statistical Analyses

All behavioral data were analyzed using either the Matlab (Release 2012b, version 8.0.0.783, (The MathWorks Inc., 2012)) or R (Version 2.14.2, (“R Core Team,” 2014)) statistical software packages.

General linear model for RT

We modeled reaction times in a linear mixed effects model fit by restricted maximum likelihood as a function of the binary variable Group (Stress, Control), and continuous variables of PSL and cortisol level at the subject level and the difference in health and taste between both items, the recommendation, and the type of choice a participant made with regard to taste and health (binned by higher and lower health and taste combinations) at the trial level. The model included all one, two, and

three way interactions between subject level variables and the three trial level variables (see Table S2 for full the listing). For clarity we present the model with only trial level variables below.

$$RT = \beta_0 + \beta_1 HRec + \beta_2 MHLT + \beta_3 LHMT + \beta_4 T_{diff} + \beta_5 H_{diff} + \varepsilon$$

RT is the log transformed reaction time on each trial. HRec takes the value of 1 whenever the healthier food is recommended, 0 when there is no recommendation, and -1 when the less healthy food is recommended. MHLT is a binary regressor taking the value of 1 whenever a healthier, but less tasty food is chosen and 0 otherwise. LHMT is a binary regressor taking the value of 1 whenever a less healthy, but tastier food is chosen and 0 otherwise. T_{diff} is the absolute value of the difference in taste ratings between the two foods, and H_{diff} is the absolute value of the difference in health ratings between the two foods. The subject level variables PSL and cortisol were z-scored across participants.

fMRI data acquisition

Images were acquired using a Philips Achieva 3 T whole-body scanner with an eight-channel sensitivity-encoding head coil (Philips Medical Systems) at the Laboratory for Social and Neural Systems Research, University Hospital Zurich. Stimulus presentation was controlled with the Psychophysics Toolbox Software (Psychtoolbox 3.0, (Brainard, 1997)); the paradigm was presented via a back-projection system to a mirror that was mounted on the head-coil.

We acquired gradient echo T2*-weighted echo-planar images (EPIs) with blood-oxygen-level-dependent (BOLD) contrast (41 slices per volume, Field of View 200 x 126.5 x 200 mm, slice thickness 2.5 mm, 0.6 mm gap, in-plane resolution 2.5*2.5 mm, matrix 80*80, repetition time 2460 ms, echo time 30 ms, flip angle 77°) and a SENSE reduction (i.e. acceleration) factor of 2. Volumes were acquired in axial orientation at a +15° tilt to the anterior commissure-posterior commissure line. We collected 161 volumes in ascending order during each of the three experimental runs, together with five “dummy” volumes at the start and end of each run. A T1-weighted turbo field echo structural image was acquired in sagittal orientation for each participant at the end of the scanning session with the same angulation that applied to the functional scans (181 slices, Field of View 256 x 256 x 181 mm, slice thickness 1 mm, no gap, in-plane resolution 1*1 mm, matrix 256*256, repetition time 8.4 ms, echo time 3.89 ms, flip angle 8°). To measure the homogeneity of the magnetic field we collected B0/B1

maps before the first and second run and before acquiring the structural scan (short echo time = 4.29 ms, long echo time = 7.4 ms). We measured breathing frequency and took an electrocardiogram with the in-built system of the scanner in order to correct for physiological noise.

fMRI Preprocessing

Statistical parametric mapping (SPM8, Update Rev. Nr. 5236; Functional Imaging Laboratory, University College London) was used to spatially realign and unwarp functional data, segment them according to the corresponding T1-weighted high resolution structural image and normalize them to the participant's mean EPI template. Images were smoothed using an isometric Gaussian kernel (4 mm full width at half maximum). As physiological noise may disturb the BOLD signal and account for fluctuations, we used RETROICOR, as implemented in the PhysIO toolbox, to model respiration and heartbeat (Glover et al., 2000). The implementation of RETROICOR we used, the PhysIO Toolbox (Kasper, 2009), is open source code available as part of the TAPAS software collection: www.translationalneuromodeling.org/tapas/. This algorithm uses Fourier expansions of different order for the estimated phases of cardiac pulsation (3rd order), respiration (4th order) and cardio-respiratory interactions (1st order) following (Harvey et al., 2008). For two participants, physiological data from the scan were not saved due to a technical problem. For these participants, we applied only the standard motion correction procedure as implemented in SPM 8.

Figures for depicting the fMRI results were created with the MRICron (<http://www.mccauslandcenter.sc.edu/mricro/mricron/>) and MRICro GL software (<http://www.mccauslandcenter.sc.edu/mricrogl/>; (Rorden and Brett, 2000)).

Augmented GLM-health, taste value (HT-FVdiff)

In GLM-HT-FVdiff, we augmented our GLM-HT to examine the effects of health, taste, and recommendations on BOLD activity using a model with regressors identifying five events of interest: 1) all choice onsets, 2) trials in which the healthier food was recommended and chosen, 3) trials in which the healthier food was recommended and not chosen, 4) trials in which the less healthy food was recommended and chosen, 5) trials in which the less healthy food was recommended and not chosen. In this augmented version that accounts for the discriminability of the food options, five parametric

modulators were included with the first regressor for all choices: P1) Difference between the chosen and non-chosen food value (FVdiff), P2) Health rating for chosen item (Hc), P3) Taste rating for chosen item (Tc), P4) Health rating for non-chosen item (Hnc), P5) Taste rating for non-chosen item (Tnc). These parametric regressors were orthogonalized with respect to one another. All regressors were defined as boxcar functions with duration equal to the reaction time on that trial. Regressors for head motion, cardiac, and respiratory effects were included to account for BOLD signal variability associated with these effects.

Following the estimation of GLM-HT for each participant, we computed first level contrasts for: 1) Tc-Tnc, 2) FVdiff. Next, we computed a two-sample t-test between the Stress and Control groups comparing the relative taste value (Tc-Tnc) and food value difference (FVdiff) signals. In the relative taste value analysis, we corrected for multiple comparisons within the same anatomically defined ROI as in GLM-HT, encompassing all voxels with a non-zero probability of belonging to the bilateral amygdalae or nucleus accumbens as defined by the Harvard-Oxford subcortical atlas (Desikan et al., 2006).

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